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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/079,035	02/19/2002	John Andrew Ryals	21212C	7909

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EXAMINER	
KUBELIK, ANNE R	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 11/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application N .	Applicant(s)	
	10/079,035	RYALS ET AL.	
	Examin r	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. As requested in the amendment filed 19 February 2002, claims 1-32 have been cancelled. Claims 33-46 are pending.

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825.

Sequence identifiers are missing from either the legend or the Brief Description of Fig. 8.

Full compliance with the sequence rules is required in response to this Office action. A complete response to this Office action must include both compliance with the sequence rules and a response to the issues set forth herein. Failure to fully comply with both of these requirements in the time period set forth in this Office action will be held to be non-responsive.

Claim Objections

3. Claim 43 is objected to because of the following informalities:

Claim 43 is not written in proper Markush format. The claim should be in the format "selected from the **group consisting of** A, B, C and D." The word and punctuation "following:" should be replaced with --group consisting of--. See MPEP 2173.05(h).

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 33-36 and 39-46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids of SEQ ID NO:2 or encoding SEQ ID NO:3, plants transformed with them, and a method of using them to increase SAR gene expression or enhance disease resistance in a transgenic plant, does not reasonably provide enablement for nucleic acids that hybridize to SEQ ID NO:2, plants transformed with them, and a method of using them to increase SAR gene expression or enhance disease resistance in a transgenic plant. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to isolated DNA molecules that encode proteins involved in the signal transduction cascade leading to systemic acquired resistance (SAR) in plants and that hybridize to SEQ ID NO:2 under moderately stringent conditions. The claims are also drawn to plants transformed with those DNA molecules and methods of using those DNA molecules to increase SAR gene expression and enhance disease resistance in a plant.

The instant specification, however, only describes mutation of Arabidopsis plants and isolation of *nim* mutant plants that did not have resistance to *Peronospora parasitica*, even when sprayed with SA, INA or BTH, in comparison to NahG plants (examples 1-3); northern analysis of Pr-1, -2 and -5 gene expression in the mutant plants (example 4); analysis of SA accumulation (example 5); genetic analysis of the mutants to show that the mutants fell into t two complementation groups (example 6), mapping the NIM1 locus and isolation of the NIM1 gene, SEQ ID NO:1 (examples 7-11); determination of the mutations in the other mutants (example 12); complementation and Northern analysis to confirm that this gene corresponds to the

mutation (example 13-14), isolation of the NIM1 cDNA (SEQ ID NO:2) (example 15); transformation of plants with constructs comprising the NIM1 gene to show that they had increased resistance to pathogens (examples 18-19). The specification also prophetically discusses the isolation of homologous genes from other plants (example 17); generation of NIM1 deletion fragments (example 20), assessment of the CIM1 phenotype of the transformants (example 21), transformation of crop plants (example 22); use of *nim* mutants in crop and disease resistance testing, plant-pathogen interaction research, and fungicide screening (example 23-26).

The instant specification, however, fails to provide guidance for making isolated DNA molecules that encode proteins involved in the signal transduction cascade leading to systemic acquired resistance (SAR) in plants and that hybridize to SEQ ID NO:2 under moderately stringent conditions, and thus fail to provide guidance for plants transformed with those DNA molecules and methods of using those DNA molecules to increase SAR gene expression and enhance disease resistance in a plant.

Making "conservative" substitutions (*e.g.*, substituting one polar amino acid for another, or one acidic one for another) does not produce predictable results. Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252) showed that the "conservative" substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitutions with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically

reduced enzyme activity (see Table 1). The nucleic acids encoding all these mutated proteins, however, would hybridize under high stringency to the nucleic acids encoding the original protein.

The specification fails to teach how to assay nucleic acids that hybridize to SEQ ID NO:2. The recited function of the proteins encoded by these nucleic acids is that they are involved in the signal transduction cascade leading to SAR in plants. Many different proteins are involved in this process and they each have a different activity. Ryals et al (1996, Plant Cell 8:1809-1819) review a number of mutants that are involved in the signal transduction pathway leading to SAR (Figure 2); because these mutants complement one another, the genes must each encode a protein with a different activity. Similarly, Ward et al (1991, Plant Cell 3:1085-1094) teach that the expression of at least nine genes is induced in the SAR response (pg 1088, right column, paragraph 2); because their expression is induced, they are also involved in the signal transduction pathway. Thus, there is no single function for nucleic acids "involved in the signal transduction cascade leading to systemic acquired resistance in plants" and it is unclear how to assay the claimed nucleic acids.

Claim 41 is drawn to a host transformed with a chimeric gene comprising the claimed nucleic acid. The specification does not teach transformation of animals, and provides no use for animals transformed with the claimed nucleic acid. Furthermore, a human, which would be encompassed by "host", is not patentable subject matter.

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate isolated DNA molecules that encode proteins involved in the signal transduction cascade leading

to SAR in plants and that hybridize to SEQ ID NO:2 under moderately stringent conditions, plants transformed with those DNA molecules, and methods of using those DNA molecules to increase SAR gene expression and enhance disease resistance in a plant.

6. Claims 33-36 and 39-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a multitude of nucleic acids that hybridize to SEQ ID NO:2 and that encode proteins involved in the signal transduction cascade leading to systemic acquired resistance. In contrast, the specification only describes a coding sequence from *Arabidopsis* that comprises SEQ ID NO:2. Applicant does not describe other DNA molecules encompassed by the claims, and the structural features that distinguish all such nucleic acids from other nucleic acids are not provided.

The function recited of the proteins encoded by these nucleic acids is that they are involved in the signal transduction cascade leading to SAR in plants. Many different proteins are involved in this process and they each have a different activity. Ryals et al (1996, Plant Cell 8:1809-1819) review a number of mutants that are involved in the signal transduction pathway leading to SAR (Figure 2); because these mutants complement one another, the genes must each encode a protein with a different activity. Similarly, Ward et al (1991, Plant Cell 3:1085-1094) teach that the expression of at least nine genes is induced in the SAR response (pg 1088, right

column, paragraph 2); because their expression is induced, they are also involved in the signal transduction pathway.

Hence, Applicant has not, in fact, described nucleic acids that hybridize to SEQ ID NO:2 and that encode proteins involved in the signal transduction cascade leading to systemic acquired resistance within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

See *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997) at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.
> ... A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.
> ... the claimed genera of vertebrate and mammal cDNA are not described by the general language of the '525 patent's written description supported only by the specific nucleotide sequence of rat insulin.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 33-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention.

Claim 33 is indefinite in its recitation of "the coding sequence set forth in SEQ ID NO:2". A particular DNA has 6 reading frames and each has at least one open reading frame. Thus, it is not clear to which coding sequence the claim refers.

Claim 33 is indefinite in its recitation of "(X3)" and "(X1)". It is not clear what these refer to.

In claim 44 it is not clear if the seed is transgenic because it comprises the chimeric gene or if it transgenic because it has been transformed with some other nucleic acid.

9. Claims 45-46 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The methods are those of increasing SAR gene expression or enhancing disease resistance in a transgenic plant. However, the only method step is one of expressing a chimeric gene in the plant. The omitted steps are those involved in getting the chimeric gene into the plant.

Double Patenting

10. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

11. Claims 37-38 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 2-3 of prior U.S. Patent No. 6,091,004. This is a double patenting rejection.

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 33-36 and 39-46 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of U.S. Patent No. 6,091,004. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, *e.g.*, *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Although the conflicting claims are not identical, they are not patentably distinct from each other because nucleic acids encoding SEQ ID NO:3, of SEQ ID NO:2, or comprised within

clone BAC-04, plants transformed with those nucleic acids, and methods of using them to increase SAR gene expression and enhance disease resistance, as claimed in the issued patent, are species of the genus of nucleic acids that hybridize to SEQ ID NO:2, plants transformed with those nucleic acids, and methods of using them to increase SAR gene expression and enhance disease resistance, as claimed in the instant application.

14. Claims 33-46 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 5,986,082. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, *e.g.*, *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the isolated nucleic acid claimed in the issued patent (SEQ ID NO:7) is 87.1% similar to the isolated nucleic acid claimed in the instant application (see sequence search results) and would thus hybridize to it under the conditions recited in the instant claim 33. Thus, this nucleic acid, plants transformed with it, and methods of using it to increase SAR gene expression and enhance disease resistance, as claimed in the issued patent, is a species of the genus of nucleic acids that hybridize to SEQ ID NO:2, plants transformed with those nucleic acids, and methods of using them to increase SAR gene expression and enhance disease resistance, as claimed in the instant application.

15. Claims 45-46 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-32 of U.S. Patent No. 6,031,153. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, *e.g.*, *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Although the conflicting claims are not identical, they are not patentably distinct from each other because methods of protecting a plant from pathogen attack comprising transformation with a nucleic acid encoding NIM1, as claimed in the issued patent, are species of the genus of methods of using nucleic acids that hybridize to SEQ ID NO:2 to increase SAR gene expression and enhance disease resistance, as claimed in the instant application. That is because the instantly claimed method must be practiced in order to practice the method claimed in the issued application.

16. Claims 33-46 are free of the prior art, given the failure of the prior art to teach an isolated nucleic acid that hybridizes to SEQ ID NO:2.

Conclusion

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0198.

Anne R. Kubelik, Ph.D.
November 20, 2003